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Once Nocturia, Always Nocturia? Natural History of Nocturia in Older Men Based on Frequency-Volume Charts: The Krimpen Study

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Abbreviations and Acronyms

DAN-PSS-1 = Danish Prostatic Symptom Score

FU = followup

FVC = frequency-volume chart

GP = general practitioner

ICS = International Continence Society

I-PSS = International Prostate Symptom Score

NVF = nocturnal voiding frequency

PY = person-years

TAMUS = Tampere Aging Male Urologic Study

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Purpose: Nocturia is a highly prevalent and bothersome symptom that might (spontaneously) resolve. However, longitudinal data are not available on the incidence and resolution of nocturia assessed with frequency-volume charts. In this study we determined the prevalence, incidence and resolution rates of nocturia assessed by frequency-volume charts, and compared nocturnal voiding frequency over time as assessed by frequency-volume charts and questionnaires.

Materials and Methods: A longitudinal, population based study was conducted among 1,688 men 50 to 78 years old with followup rounds at 2.1, 4.2 and 6.5 years. Nocturnal voiding frequency was determined with frequency-volume charts and, for comparison purposes, with a question from the International Prostate Symptom Score. Nocturia was defined as nocturnal voiding frequency 2 or greater. Prevalence, incidence and resolution rates were also determined.

Results: At the 2.1-year followup the incidence rate was 23.9% and the resolution rate was 36.7%. The incidence rate was highest in the oldest group (70 to 78 years) and lowest in the youngest (50 to 54 years), whereas the resolution rate was highest in the group 55 to 59 years old and lowest in the oldest group. Because of the high resolution rate, no reliable incidence rates can be calculated. Despite fluctuation, the prevalence of nocturia increased with age and over time (from 34.4% to 44.7% for the total group, $p < 0.05$). Men who had a frequency-volume chart–nocturnal voiding frequency less than International Prostate Symptom Score–nocturnal voiding frequency (6% of the population) more often had this later on.

Conclusions: In this population frequency-volume chart assessed nocturia shows considerable fluctuation. Nevertheless, prevalence increases over time and with increasing age. Men who once had frequency-volume chart–nocturnal voiding frequency less than International Prostate Symptom Score–nocturnal voiding frequency are more likely to have this again. Therefore, frequency-volume charts as well as the International Prostate Symptom Score should be used when evaluating nocturia.

Key Words: nocturia, prevalence, urinary tract physiological phenomena, incidence, data collection

NOCTURIA is a condition for which terminology was standardized by the ICS in 2002.[1,2] It is reported that less than 2 voids each night seem to generate no bother and that 2 or more voids give rise to impaired quality of life.[3–5] Because of different definitions used in earlier studies and various ways of assessing NVF, eg questionnaires or FVCs, a range of prevalence rates have been reported.[6,7]

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Nevertheless, the prevalence of nocturia in community dwelling older men increases with age. Furthermore, nocturia is the most bothersome lower urinary tract symptom.[8,9]

Longitudinal data on the course of nocturia in community dwelling men are limited to TAMUS, which showed fluctuation of nocturia in individuals over time.[3] The value of this information for daily practice is uncertain for several reasons. TAMUS is based on the DAN-PSS-1 questionnaire,[10] which fails to emphasize the important point of getting out of bed to void at night and, therefore, does not comply with the ICS definition of nocturia.[2] In addition, because of the DAN-PSS-1 response categories the exact NVF could not be determined.[11] It is also unclear whether fluctuation is an effect of the assessment tool used. FVCs represent a different, possibly more objective, method of assessing nocturia because no recall bias is involved.[12] Furthermore, the correlation between questionnaire data and FVCs is only modest[13] and, until now, no longitudinal data have been available on FVC assessed nocturia. Therefore, in this study we determine the prevalence, incidence and resolution rates of nocturia based on FVCs in community dwelling older men. The longitudinal relation between NVF as assessed with FVCs and with questionnaires is also examined.

MATERIALS AND METHODS

The Krimpen study is a longitudinal study on urogenital tract dysfunction and its impact on general health status. The design of this institutional review board approved study has been described elsewhere.[13,14] All men age 50 to 78 years (reference date June 1995, sample size 3,924) in the Dutch municipality Krimpen aan den IJssel were investigated. Exclusion criteria for participation were transurethral or open prostatectomy, prostate or bladder cancer, neurogenic bladder disease, or negative advice from their GP based on poor health (eg bedridden). At baseline participants completed a 113-item questionnaire, including the I-PSS, and visited the local GP health center for medical examination. Then urological measurements were performed at the urological outpatient department of the Erasmus Medical Centre Rotterdam and participants completed a 3-day FVC.

Followup

The followup rounds were performed after an average interval of 2.1, 4.2 and 6.5 years.[15] If the participant had not died or moved away and no exclusion criteria were met, the GPs were asked to send a re-invitation letter for a first, second and third followup round. Men who had undergone lower urinary tract surgery during followup were censored. Additionally, for the third followup round all nonresponders of the previous rounds were re-invited.

Nocturia Determined From FVCs

On the 3-day FVC participants recorded each micturition in 1-hour time units (first 2 days) and the volume of each void (third day). Times of rising and bedtime were also noted. Fluid intake was not recorded. Retrospectively this complies with the 2002 ICS definition of a FVC.[1]

We determined the 24-hour voiding frequency from the FVC. Since nocturia is defined as getting out of bed to void, NVF was determined from bedtime to time of rising. This method is more accurate than using fixed sleeping times, which leads to significant misclassification of NVF.[16] A minimum of 4 recorded sleeping hours was required for inclusion as an adequately completed FVC. NVF was estimated as the mean of 2 nights (when available) or the frequency of 1 night to allow analyses of as many participants as possible.

Nocturia, Incidence and Resolution

Nocturia was defined as a NVF of 2 or greater. Resolution was defined as nocturia at baseline but no nocturia at followup 1 (FU-1). The incidence rate was determined by dividing the number of new cases of nocturia at FU-1 by the total number of participants without nocturia at baseline. The resolution rate was determined by dividing the number of men who did not have nocturia at FU-1 by the number of men who had nocturia at baseline.

Nocturia From I-PSS Questionnaire

We used the I-PSS nocturia question to determine I-PSS–NVF. I-PSS–NVF and FVC–NVF were compared by subtracting I-PSS-NVF from FVC-NVF. We defined scores of 1 or greater as FVC-NVF greater than I-PSS-NVF and scores -1 or less as FVC-NVF less than I-PSS-NVF.

Statistical Analyses

All men were divided into 5-year age strata and their general characteristics were noted. For each stratum the prevalence rate for nocturia was determined and compared throughout the FU rounds using McNemar's test. Incidence and resolution rates were also determined. Finally, the results of the FVCs were compared with I-PSS data on nocturia to establish whether men had a higher or lower estimated NVF. Statistical analyses were performed with SPSS® version 15.0 with $p < 0.05$ considered statistically significant.

RESULTS

Baseline characteristics of the study population are presented in table 1. Median patient age was 60.9 years (IQR 56.1–66.2). Most men (75.6%) had an I-PSS of 7 or less. At baseline 1,597 men (95% of the responders) completed a 3-day FVC. Because of missing data on bedtime and time of rising (372), and exclusion criteria (103), the NVF could be determined in 1,122 men at baseline (71% of the completed charts). In terms of charts 701 (74%), 360 (76%) and 302 (76%) were used for analyses in the followup rounds after 2.1 (FU-1), 4.2 (FU-2) and 6.5 years (FU-3), respectively. Scores on the I-PSS nocturia question did not differ between the men ex-

Table 1. *Baseline characteristics of study population*

No. age group (%):		
50–54	213	(19.0)
55–59	297	(26.5)
60–64	265	(23.6)
65–69	215	(19.2)
70–78	132	(11.8)
Median I-PSS (IQR)	4	(1–7)
No. I-PSS categories (%):		
None (0)	113	(10.1)
Mild (1–7)	735	(65.5)
Moderate (8–19)	246	(21.9)
Severe (20–35)	28	(2.5)
Median NVF/age group (IQR):		
50–54	1.0 (0.5–1.5)	
55–59	1.0 (0.5–1.5)	
60–64	1.5 (1.0–2.0)	
65–69	1.5 (1.0–2.0)	
70–78	2.0 (1.0–2.5)	
Overall	1.5 (1.0–2.0)	

cluded from study and those who provided exact data on sleeping hours ($p = 0.251$).

Table 2 shows the prevalence rates of nocturia (by age strata) at baseline and followup. In the total group the prevalence of nocturia increased significantly over time from 34.4% at baseline to 44.7% after 6.5 years ($p < 0.01$). After 6.5 years there was a significant increase in prevalence for all baseline age strata except for 65 to 69 years old.

Table 3 presents nocturia incidence rates (in 464) and resolution rates (in 237) after 2.1 years. The overall incidence rate was 23.9% after 2.1 years. The incidence was highest in the oldest group (70 to 78 years old) and lowest in the youngest group (50 to 54 years old). The overall resolution rate was 36.7%, being highest in the youngest group and lowest in the oldest group. The incidence rate was lower than the resolution rate. However, since the absolute number of men with incident nocturia was higher, the prevalence rate increased over time.

The figure shows the pattern of incidence and resolution of nocturia during followup. Of the men with nocturia at baseline 36.7% did not have nocturia after 2.1 years. Of the latter group 48.8% had nocturia again after 4.2 years. Of the men who had nocturia at baseline and after 2.1 years, 21.6% did not have nocturia after 4.2 years. Thus, most men who did not have nocturia at baseline did not experience during 4.2 years of followup, and of those with nocturia at baseline the majority still had nocturia after 4.2 years.

Table 3. *Incidence and resolution rates based on FVCs*

	% (95% CI)	
Age Group	Incidence	Resolution
50–54	18.6 (10.7–26.4)	59.3 (39.5–79.1)
55–59	20.4 (13.7–27.1)	46.8 (32.0–61.6)
60–64	25.7 (17.5–33.8)	32.8 (20.7–44.9)
65–69	24.4 (14.6–34.1)	30.0 (18.1–41.9)
70–78	47.1 (29.4–64.7)	26.2 (12.3–40.1)
Overall	23.9 (20.0–27.8)	36.7 (30.5–52.9)

Table 4 presents a comparison of the I-PSS and FVC data. Of the 1,122 men who completed the FVC and I-PSS at baseline, 33.3% reported a lower NVF on FVCs, 60.3% scored an equal frequency and 6.3% claimed a higher NVF on the I-PSS questionnaire than on the FVC. A lower frequency on the I-PSS nocturia question than on FVC was rarest in the youngest age group. Of the men who had FVC-NVF less than I-PSS-NVF at baseline 23.3% had this again after 2.1 years. Men who made a correct estimation or who had FVC-NVF greater than I-PSS-NVF showed a similar pattern in the subsequent followup. However, men who had FVC-NVF less than I-PSS-NVF more often had FVC-NVF less than I-PSS-NVF again in the subsequent followup. Overall, most men did not estimate I-PSS-NVF to be higher than the recorded NVF on the FVC.

DISCUSSION

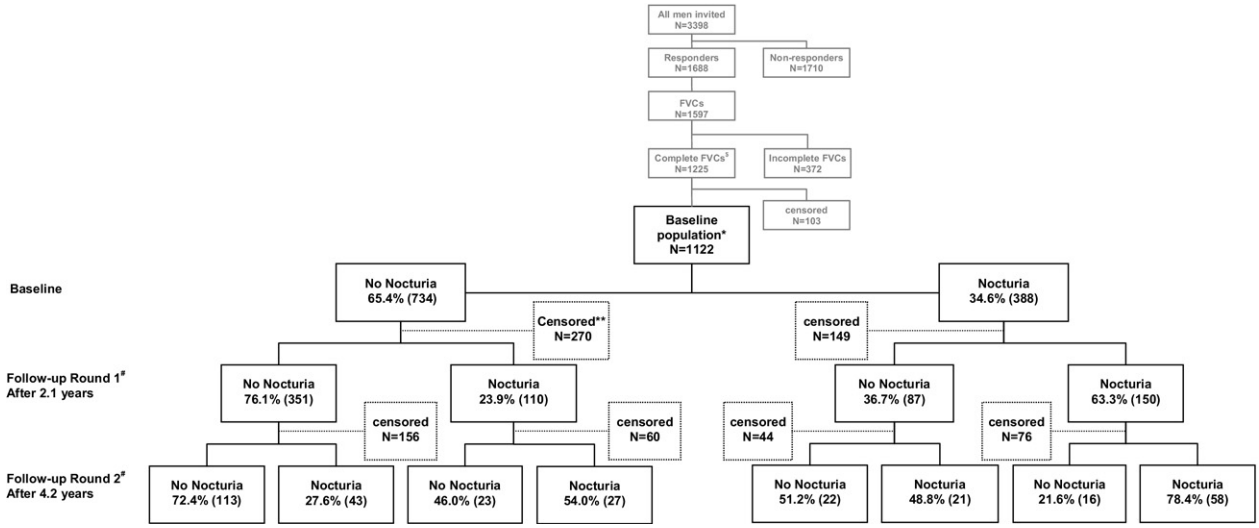
This study shows that the prevalence rate of nocturia increases with age and over time, and that the incidence and resolution rates are relatively high. Because to our knowledge this is the first report on FVC based longitudinal data on the prevalence, incidence and resolution of nocturia, a direct comparison with other studies is not possible.

TAMUS provided longitudinal data on nocturia based on questionnaires (DAN-I-PSS-1).[3] However, the methodology of that study differs from ours in

Table 2. *Prevalence of nocturia based on FVCs*

Age Group	Baseline % (95% CI)	Followup 1 % (95% CI)	Followup 2 % (95% CI)	Followup 3 % (95% CI)
50–54	19.7 (14.3–25.1)	23.4 (15.8–30.9)	39.0 (26.2–51.8)*	33.8 (22.3–45.4)*
55–59	24.6 (19.7–29.5)	28.6 (22.1–35.1)	33.0 (24.1–42.0)	34.8 (24.7–44.9)*
60–64	36.6 (30.8–42.4)	40.2 (32.9–47.6)	45.7 (35.5–56.0)	52.6 (41.2–64.1)*
65–69	46.1 (39.3–52.8)	44.2 (35.8–52.6)	60.9 (48.7–73.2)	58.7 (43.9–73.5)
70–78	56.8 (48.3–65.4)	61.8 (50.7–73.0)	55.9 (38.3–73.5)	60.9 (39.3–82.5)*
Overall	34.4 (31.6–37.2)	37.2 (33.7–40.8)	44.4 (39.3–49.6)*	44.7 (39.1–50.3)*

* McNemar's test compared to baseline, $p < 0.05$.



Flowchart showing fluctuation of nocturia (defined as 2 or more nocturnal voids) in open population of older men as declared on FVCs. Asterisk indicates all men who completed FVC and did not meet exclusion criteria at baseline. Double asterisk indicates censored or lost to followup, including men who moved out of area, did not respond to re-invitation, were deceased or met exclusion criteria. Pound sign indicates that number of men and prevalence rates do not concur with numbers in flowchart per round because in prevalence rate, men who did not complete FVC in previous rounds can be included while this is not possible in flowchart. Dollar sign indicates FVCs with reported sleeping hours.

the 5 areas of 1) inclusion criteria—specific birth years vs men in a specified age range, 2) followup period—5 vs 2.1 years, 3) definition of nocturia—categorized as mild (1 to 2 times), moderate (3 to 4) or severe (5+) vs NVF 2 or greater, 4) definition of resolution—change from any DAN-PSS-1 symptom category to a lower category vs change to NVF less than 2, and 5) assessment tool used—questionnaire vs FVC. This rules out a straightforward comparison. Moreover the DAN-PSS-1 nocturia question, "How many times do you have to urinate during the night?" does not imply that one has to get up out of bed to void.[10] Thus, the DAN-PSS-1 does not concur with the ICS definition of nocturia.[2]

Table 4. *Consistency of under estimation, correct estimation and overestimation of NVF, based on I-PSS nocturia question and FVC data with FVC used as reference*

		% Followup		
% Baseline (1,122)		FVC-NVF greater than I-PSS-NVF	FVC-NVF = I-PSS-NVF	FVC-NVF less than I-PSS-NVF
FVC-NVF greater than I-PSS-NVF:*				
Younger than 65	32.6	37.9	60.1	2.0
65 or Older	34.9	51.4	44.4	4.2
Overall	33.3	42.2	55.1	2.7
FVC-NVF = I-PSS-NVF:†				
Younger than 65	59.9	27.1	67.6	5.4
65 or Older	61.4	28.2	65.6	6.1
Overall	60.3	27.4	67.0	5.6
FVC-NVF less than I-PSS-NVF:‡				
Younger than 65	7.5	21.2	51.5	27.3
65 or Older	3.7	50.0	40.0	10.0
Overall	6.3	27.9	48.8	23.3

* NVF was estimated lower on I-PSS than on FVC.
† NVF was estimated equally high on I-PSS as on FVC.
‡ NVF was estimated higher on I-PSS than on FVC.

In the Krimpen study the incidence rate of 23.9% expressed in cases per 1,000 person-years, ie 129/1,000 PY after 2.1 years, is considerably higher than the TAMUS rate of 75/1,000 PY after 5 years. The Krimpen study resolution rate is also considerably higher than that in TAMUS (214/1,000 PY vs 35/1,000 PY). The difference in incidence and resolution might be explained by differences in the followup period. In a 5-year period nocturia in an individual might resolve but then become incident again (see figure). Furthermore, epidemiological studies have shown that a longer followup period can result in lower incidence rates in diseases with a tendency to resolve.[17] The difference in resolution rate might be due to the different response categories used in the DAN-PSS-1. For example, most men have moderate nocturia. Therefore, men who change from 2 voids to 1 void would be classified as resolved in our study, but not in TAMUS where they would remain in the same response category. Nevertheless, nocturia fluctuates over time, and this fluctuation is independent of the assessment method used. Moreover, this fluctuation implies that it is almost impossible to calculate reliable incidence rates. Preferably, future studies should try to create a sample size sufficient for a

focus on subgroups with more durable prevalence and durable resolution of nocturia.

One limitation of the present study is that we used exact sleeping hours to define the night, thereby excluding some men from the analysis. However, the scores on the I-PSS question of the excluded men did not differ from those of men with exact sleeping hour data. In addition, because the oldest age groups had fewer men with missing data on sleeping hours, this might have led to a slight overestimation of the prevalence of nocturia in the total population.

Resolution of nocturia might be due to medical treatment. Although we did not conduct a pharmacoepidemiological analysis, we believe that medical treatment does not explain the fluctuation. Our earlier study showed that only 9.5% of all participants sought medical help for LUTS.[18] Of these participants 3.1% received medical treatment, 2.6% watchful waiting and 3.8% underwent surgical treatment. Furthermore, treatment was not specifically focused on nocturia, and participants who underwent prostate surgery were censored in the current analyses. It has also been shown that nocturnal voiding frequency as a symptom in men with benign prostatic hyperplasia was reduced in only 13.9% of these men, after the start of treatment with an α-blocker.[19] In a similar study population equally low medical treatment rates for lower urinary tract symptoms were reported,[20] reflecting the conservative prescription policy of Dutch GPs. The low treatment rates also reflect the nature of our study, ie a population based study rather than a (urological) patient study. Therefore, it is highly unlikely that medical therapy for benign prostatic hyperplasia has a large mitigating effect on nocturia in our study.

In this study we also compared the NVF as estimated on the I-PSS and FVCs. About 60% of the men equally estimated their NVF with both assessment methods. Of the men with FVC-NVF less than I-PSS-NVF, a higher proportion again had a FVC-NVF less than I-PSS-NVF in the subsequent followup. This mainly occurred among men younger than 65 years old. This finding might indicate that these men are more focused on nocturia than those older than age 65 years. An explanation could be that most men older than 65 years are retired and do not have to get up early for work. However, when treating nocturia it is important to let patients complete an I-PSS and a FVC for optimal insight into actual NVF, quality of life and possible cause of nocturia (eg nocturnal polyuria).

CONCLUSIONS

Because of the high incidence and resolution rates nocturia is often a transient phenomenon. Fluctuation is seen regardless of the assessment method used. Due to this fluctuation it is almost impossible to provide reliable incidence rates of nocturia in community dwelling older men. Because fluctuation of nocturia might, in part, be due to its multifactorial etiology, it is important to further elucidate the cause(s) of nocturia. To establish the determinants of incident nocturia it is advisable to focus on incident nocturia that does not resolve in the subsequent followup round. Based on the discrepancy between NVF on FVC and I-PSS, this study also emphasizes the importance of using an FVC as a confirmatory way of assessing nocturia before considering therapeutic interventions.

REFERENCES

1. Abrams P, Cardozo L, Fall M et al: The standardisation of terminology of lower urinary tract function: report from the Standardisation Subcommittee of the International Continence Society. Neurourol Urodyn 2002; **21:** 167.
2. Van Kerrebroeck P: Standardization of terminology in nocturia: commentary on the ICS report. BJU Int 2002; **90:** 16.
3. Hakkinen JT, Hakama M, Shiri R et al: Incidence of nocturia in 50 to 80-year-old Finnish men. J Urol 2006; **176:** 2541.
4. Hernandez C, Estivill E, Prieto M et al: Nocturia in Spanish patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH). Curr Med Res Opin 2008; **24:** 1033.
5. Tikkinen KA, Johnson TM 2nd, Tammela TL et al: Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. Eur Urol 2009; **57:** 488.
6. Bosch JL and Weiss JP: The prevalence and causes of nocturia. J Urol 2010; **184:** 440.
7. Markland AD, Vaughan CP, Johnson TM 2nd et al: Prevalence of nocturia in United States men: results from the National Health and Nutrition Examination Survey. J Urol 2011; **185:** 998.
8. Andersson SO, Rashidkhani B, Karlberg L et al: Prevalence of lower urinary tract symptoms in men aged 45-79 years: a population-based study of 40 000 Swedish men. BJU Int 2004; **94:** 327.
9. Coyne KS, Zhou Z, Bhattacharyya SK et al: The prevalence of nocturia and its effect on health-related quality of life and sleep in a community sample in the USA. BJU Int 2003; **92:** 948.
10. Tibaek S and Dehlendorff C: Validity of the Danish Prostate Symptom Score questionnaire in stroke. Acta Neurol Scand 2009; **120:** 411.
11. Meyhoff HH, Hald T, Nordling J et al: A new patient weighted symptom score system (DAN-PSS-1). Clinical assessment of indications and outcomes of transurethral prostatectomy for uncomplicated benign prostatic hyperplasia. Scand J Urol Nephrol 1993; **27:** 493.
12. Bright E, Drake MJ and Abrams P: Urinary diaries: evidence for the development and validation of diary content, format, and duration. Neurourol Urodyn 2011; **30:** 348.
13. Blanker MH, Bohnen AM, Groeneveld FP et al: Normal voiding patterns and determinants of increased diurnal and nocturnal voiding frequency in elderly men. J Urol 2000; **164:** 1201.

14. Blanker MH, Groeneveld FP, Prins A et al: Strong effects of definition and nonresponse bias on prevalence rates of clinical benign prostatic hyperplasia: the Krimpen study of male urogenital tract problems and general health status. BJU Int 2000; **85:** 665.

15. Kok ET, Groeneveld FP, Busschbach JJ et al: Influence of coping styles on quality of life in men with new and increasing lower urinary tract symptoms. The Krimpen Study in community-dwelling men. Urol Int 2007; **79:** 226.

16. Blanker MH, Bernsen RM, Bosch JL et al: Relation between nocturnal voiding frequency and nocturnal urine production in older men: a population-based study. Urology 2002; **60:** 612.

17. Schouten BW, Bosch JL, Bernsen RM et al: Incidence rates of erectile dysfunction in the Dutch general population. Effects of definition, clinical relevance and duration of follow-up in the Krimpen Study. Int J Impot Res 2005; **17:** 58.

18. Kok ET, Bohnen AM, Bosch JL et al: Patient's quality of life and coping style influence general practitioner's management in men with lower urinary tract symptoms: the Krimpen Study. Qual Life Res 2006; **15:** 1335.

19. Yoshimura K, Ohara H, Ichioka K et al: Nocturia and benign prostatic hyperplasia. Urology 2003; **61:** 786.

20. Verhamme KM, Dieleman JP, Bleumink GS et al: Treatment strategies, patterns of drug use and treatment discontinuation in men with LUTS suggestive of benign prostatic hyperplasia: the Triumph project. Eur Urol 2003; **44:** 539.